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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	16

DATE MAILED: 11/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/769,223	Applicant(s) BENVENISTE ET AL.	
	Examiner Jeffrey S. Parkin, Ph.D.	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17,20,32,33 and 40-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17,20,32,33 and 40-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *15* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Amendment

Status of the Claims

1. Acknowledgement is hereby made of receipt and entry of the amendment filed 11 August, 2003, wherein claims 17, 32, and 33 were amended and new claims 40-44 introduced. Claims 17, 32, 33, and 40-44 are pending in the instant application.

Information Disclosure Statement

2. The information disclosure statement filed 11 August, 2003, has been placed in the application file and the information referred to therein has been considered. Applicants are advised the latter submission was a duplicate of the former submission and the references cited therein were already considered.

35 U.S.C. § 112, First Paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 17, 32, 33, and 40-44 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed toward methods of vaccinating humans against HIV infection by administering an immunogen that induces a protective immune response. Specifically, the immunogen must induce a cell-mediated immune response without inducing a humoral response. Additional

limitations stipulate that the immunogen must comprise an inactivated HIV carrying a NC deletion. The term "vaccine" has an art-recognized definition and refers to a preparation capable of inducing a protective or therapeutic immune response (see Dorland's Illustrated Medical Dictionary, 1988, and Stedman's Medical Dictionary, 1982). Applicants argue that the invention as claimed is fully enabled by the disclosure. These arguments have been carefully considered but are not deemed to be persuasive for the reasons of record previously set forth in paper no. 12.

As previously disclosed, the legal considerations that govern enablement determinations pertaining to undue experimentation are disclosed in *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988) and *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) The disclosure still fails to provide adequate guidance pertaining to the ability of any given immunogen to induce a cell-mediated immune response without generating a noticeable humoral response. Applicants' response failed to provide any evidence or publications that would obviate this aspect of the rejection. As previously noted, a recent publication (Shearer and Clerici, 1997) clearly noted that "the conditions under which some of these parameters result in a preferential response of one type or the other have not yet been determined." There are several factors

governing the immune response to any given immunogen (i.e., immunogen dose, adjuvant selection, route of immunization, structure of immunogen, type of antigen presenting cells, costimulatory signals, vaccinee genetic background, cytokine environment, vaccinee immunologic status) thereby making the immunization process an empirical one at best. Since all of these factors can influence the immune response, the skilled artisan cannot readily predict how any given putative vaccine will influence the immune response. Extensive testing will be required to ascertain which of the aforementioned parameters are most important. Unfortunately, the disclosure fails to address this point as it applies to humans and putative HIV vaccines.

2) The disclosure fails to provide adequate guidance pertaining to the nature of the immunogen. Applicants fail to proffer any evidence or publications that address this limitation. The disclosure clearly fails to identify suitable HIV-1 or -2 immunogens. This is not surprising considering that **the correlates of protective immunity pertaining to HIV-1 infection have not been determined** (see point 4, below).

3) The disclosure fails to provide any working embodiments. Applicants' response did not contain any declaratory data or relevant scientific publications that address this defect. As previously set forth, the specification is prophetic and fails to provide any data suggesting the HIV immunogens of interest are actually capable of inducing a protective or therapeutic immune response. The inventors report that the invention is predicated upon the finding that the low dose administration of an SIV immunogen leads to a strong and long-term protective cell-mediated immune response. However, as set forth below (see point 4), SIV is not an art-recognized animal model for HIV-1 or -2 vaccine development. Thus, any findings obtained from such studies cannot be directly extrapolated to HIV and humans. Moreover, the SIV

study of interest failed to set forth any concrete details pertaining to the factors discussed in point 1.

4) The state-of-the-art vis-à-vis HIV vaccine development has encountered many difficulties and failures (Hoth *et al.*, 1994; Stott and Almond, 1995; Graham and Wright, 1995; Haynes *et al.*, 1996; Haynes, 1996; Kent *et al.*, 1997; Lee, 1997; Letvin, 1998; Burton and Moore, 1998; Moore and Burton, 1999; Nathanson and Mathieson, 2000; Johnston, 2000; Bende and Johnston, 2000; Feinberg and Moore, 2002). **To date, there is no effective vaccine for the prevention or treatment of HIV-1 or -2 infection.** This is due to a number of factors including the *quasispecies* nature of HIV infection which leads to rapid immune escape, a lack of understanding of the correlates of protective immunity thereby precluding the identification of suitable viral immunogens, delivery vehicles, and immunization regimens, the lack of suitable animal models in which to assess vaccine efficacy, the ability of the virus to reside in quiescent T-lymphocytes thereby persisting indefinitely, and a lack of understanding of mucosal immune responses. The disclosure fails to provide any illumination on any of these topics. Once again, applicants' response clearly fails to overcome this portion of the rejection.

5) The claims are of considerable breadth and encompass any given immunogen without providing sufficient structural and functional guidance. Moreover, considering the unpredictability of the state-of-the-art vis-à-vis HIV vaccine development the skilled artisan would reasonably conclude that the disclosure fails to support the breadth of the claimed invention. Applicants' response failed to adduce any evidence that would remedy this defect.

Thus, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

Finality of Office Action

5. Applicants' amendment necessitated any and all new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). **A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED,. AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.**

Correspondence

6. Correspondence related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Official communications should be directed toward one of the following Group 1600 fax numbers: (703) 308-4242 or (703) 305-3014. Informal communications may be submitted directly to the Examiner through the following fax number: (703) 308-4426. Applicants are encouraged to notify the Examiner prior to the submission of such documents to facilitate their expeditious processing and entry.

7. Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (703) 308-2227. The examiner can normally be reached Monday through Thursday from 8:30 AM to 6:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisors, James Housel or Laurie Scheiner, can be reached at (703) 308-4027 or (703) 308-1122, respectively. Any

inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1648

31 October, 2003

LAURIE SCHEINER
PRIMARY EXAMINER